

REMARKSI. Application Status

Claims 1-203 are pending in the instant application. Claim 204 has been canceled without prejudice. Claims 4, 5, 32, 44, 64, 66, 67, 71, 99, 131, 133, 134, 138, 160, 161, 166, 198 and 200- 201 have been amended. Claims 1-201 and 203 stand rejected. Claim 202 has been indicated as being allowable.

II. Amendments1) Specification

Amendments to the specification are to correct clerical errors only, and add no new matter. Specifically, the specification was amended to remove the word "be" between "alkyl" and "substituted" in the descriptions of formulae I, III and V. In addition, the typographic error at page 44, lines 18-20 has been corrected according to the Examiner's helpful suggestion.

2) Claims

Amendments to the claims corrected inadvertent discrepancies between claim dependencies. Further amendments corrected clerical errors in the recitation of C<sub>1</sub>-C<sub>5</sub> alkyl groups. As written, there was no literal antecedent basis in these claims for "said C<sub>1</sub>-C<sub>5</sub> alkyl," since the claim recited a "C<sub>1</sub>-C<sub>3</sub> alkyl" previously.

### III Specific Grounds for Rejection

#### A. Claim Objection

##### **3) Objection to claim 204**

Claim 204 was objected to as being a substantial duplicate of Claim 202. Claim 204 has been canceled without prejudice, and therefore this objection is believed to be rendered moot.

##### **B) Claims rejected under 35 U.S.C. § 112, second paragraph**

**4)** Claim 66 stands rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Claim 66 has been amended to depend from claim 58 rather than claim 59, and therefore it is believed that the appropriate antecedent basis for “R<sup>3</sup> is C<sub>1</sub> to C<sub>5</sub> alkyl” is now present.

**5)** Claims 131 and 132 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Claim 131 has been amended to depend from claim 125, and thus it is believed that the appropriate antecedent basis for “R<sup>3</sup> is C<sub>1</sub> to C<sub>5</sub> alkyl” in claim 131, as amended, and “R<sup>3</sup> is methoxymethyl” in claim 132, as amended, is now present.

**6)** Claim 134 stands rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Claim 134 has been amended to depend from claim 133, which in turn depends from claim 125, and thus it is believed that the appropriate antecedent basis for “R<sup>3</sup> is methyl” in claim 134, as amended, is now present.

7) Claims 198-201 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Claims 198 and 200 have been amended to depend from claim 192, and thus it is believed that there is appropriate antecedent basis for "R<sup>3</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl substituted by alkoxy" in claim 198, "R<sup>3</sup> is methoxy methyl" in claim 199, "R<sup>3</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl" in claim 200, and "R<sup>3</sup> is methyl" in claim 201.

**C) Claims rejected under 35 U.S.C. § 102(b)**

8) Claims 1-12, 19-23, 31-40, 50, 58, 66-79, 89, 97-107, 114-118, 125, 133-146, 153-156, 164-174, 181-184, 192, 200, 201 and 203 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Currie et al. (WO 95/25717-A1). For the following reasons, the rejection is respectfully traversed, and reconsideration of the claims is requested.

A genus that embraces an undisclosed species or small subgenus will only anticipate that species or subgenus only if the species can "AT ONCE ENVISAGED" from the formula (MPEP § 2131.02). Currie et al. provides a large number of potential compounds, none of which are exemplified. There is no guidance to one of ordinary skill in the art to arrive at the compounds of the instant invention. More specifically, Currie et al. does not teach or suggest the 3-hexenoic and hexynoic acid compounds of the present invention. In fact, other than the generic definition of the substituent "X," no unsaturated carbon chains are exemplified. Therefore, it is respectfully requested that the rejection under 35 U.S.C. § 102(b) be withdrawn.

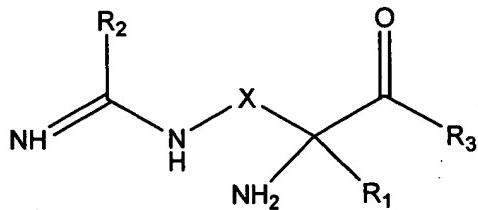
**D) Claims Rejected under 35 U.S.C. § 103(a)**

9) Claims 1-201 and 203 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Currie et al. (WO 95/25717-A1) and further in view of Hallinan et al. (US 6,334,483). For the following reasons, this rejection is respectfully traversed.

**i. Currie et al. does not suggest the instant invention**

Currie et al. does not teach or suggest the six carbon, 3 vinyl and 3 acetylene compounds of the present invention. In fact, other than the generic definition of the substituent "X," no unsaturated carbon chains are exemplified.

Currie et al. describes, at Page 4, line 1 to page 5, line 10, a large number of compounds embraced by the generic formula (I):



Currie does not, however, exemplify double or triple bonds in the carbon chain.

**See MPEP § 2144.08 Obviousness of Species When Prior Art Teaches Genus**

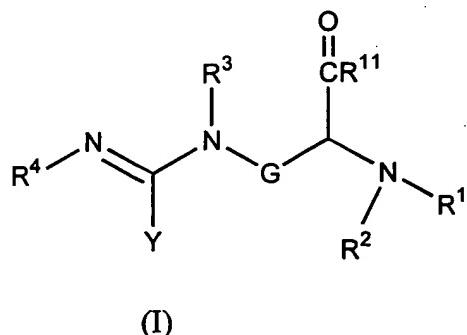
The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994) ("The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious."); *In re Jones*, 958 F.2d 347, 350, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992) (Federal Circuit has "decline[d] to extract from *Merck & Co. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir. 1989)] the rule that... regardless of how broad, a disclosure of a chemical genus renders obvious any species that happens to fall within it."). See also *In re Deuel*, 51 F.3d 1552, 1559, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995).

In the instant case, Currie et al. does not direct one skilled in the art to make the

instantly claimed compounds. No example in Currie et al. has a double bond in any position of the carbon chain.

ii Hallinan et al. does not teach or suggest the present invention

Hallinan et al. describes compounds of the general formula:



Hallinan et al. does not teach an alpha alkyl group in the carbon chain.

Moreover, of the thirty-two exemplary compounds described in Hallinan et al., only one example describes a double bond (Example 7, column 18, page 10). This example shows a 2-fluoro hex-4-enoic acid, that is, a fluorine at the N-terminal end of the carbon chain. Similarly, there is only one example of a triple-bonded carbon chain in Hallinan et al. (Example 8, column 19, page 11). Again, this compound shows a 2-fluorohex-4-yoic acid, that is, a fluorine at the N-terminal end of the carbon chain.

Hallinan et al. does not teach or suggest the halogenated compounds of the present invention, where the halogen substitutions are only provided at the double bond (that is, at the 3 or 4 position), or at a substituent at the alpha carbon. Therefore, one skilled in the art is not guided by Hallinan et al. to make the compounds claimed in the instant application.

iii Currie et al. in light of Hallinan et al. does not teach or suggest the instant invention

Currie et al. does not exemplify double or triple bonds in the carbon chain. Hallinan et al. does not teach or suggest alpha alkyl compounds. There is no motivation

to combine the teachings of Currie et al. with Hallinan et al. Although Hallinan et al., at column 3, line 3) refers to Currie et al., along with eleven other references, the Currie et al. reference is in the "Background of the Invention," and thus are distinguished from the invention described and claimed in Hallinan et al..

**iv One of ordinary skill in the Art would not be motivated to combine Currie et al. with Hallinan et al.**

The instant specification provides the following background at page 3, lines 1-6:

Various attempts have been made to improve the potency and selectivity of NOS inhibitors by adding one or more rigidifying elements to the inhibitor's structure. Publications by Y. Lee et al (Bioorg. Med. Chem. 7, 1097 (1999)) and R. J. Young et al (Bioorg. Med. Chem. Lett. 10, 597 (2000)) teach that imposing conformational rigidity with one or more carbon-carbon double bonds is not a favorable approach to impart selectivity for NOS inhibitors.

Thus, at the time of filing of the instant application, at least two literature references were available that taught against the use of carbon-carbon double bonds, such as those taught in the instant application. However, unexpectedly, the addition of carbon-carbon double bonds in this case added improved potency as compared with the compounds exemplified by Currie et al.

Therefore, one skilled in the art, at the time of the filing of the application, would not have been motivated to combine the carbon-carbon double (or triple) bonds disclosed in Hallinan et al. with the compounds disclosed in Currie et al.

**v. Hallinan et al. is commonly assigned, and not available as prior art more than one year from the filing of the instant application priority date**

Hallinan et al. was filed on January 31, 2000, and has a 102(e) date of January 31, 2000. The PCT publication date for Hallinan et al. was September 16, 1999. The instant application was filed on September 15, 2001, based upon a provisional application filed